



**University of
Zurich**^{UZH}

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2016

Prevalence and characteristics of coronary artery anomalies detected by coronary computed tomography angiography in 5 634 consecutive patients in a single centre in Switzerland

Gräni, Christoph ; Benz, Dominik C ; Schmied, Christian ; Vontobel, Jan ; Possner, Mathias ; Clerc, Olivier F ; Mikulicic, Fran ; Stehli, Julia ; Fuchs, Tobias A ; Pazhenkottil, Aju P ; Gaemperli, Oliver ; Kaufmann, Philipp A ; Buechel, Ronny Ralf

Abstract: STUDY PRINCIPLES Coronary computed tomography angiography (CCTA) allows three-dimensional visualisation of the origin, course and ending of the coronary vessels with high spatial resolution, yielding an accurate depiction of coronary artery anomalies (CAAs). This study sought to determine the prevalence, incidence and characteristics of CAAs detected with CCTA in a single centre in Switzerland. METHODS CAAs were retrospectively identified in 5 634 consecutive patients referred for CCTA between March 2007 and July 2015. Single coronary arteries, Bland-White-Garland syndrome, anomalous coronary arteries originating from the opposite site of the sinus of Valsalva (ACAOS) with an interarterial course and coronary artery fistulas were classified as potentially malignant CAAs. RESULTS We identified 145 patients with CAAs, resulting in an overall prevalence of 2.6% and cumulative incidence of 2.1% in all patients referred for CCTA in the observation period. Forty-nine (33.8%) patients showed malignant CAAs including 1 (0.7%) patient with Bland-White-Garland syndrome, 7 (4.8%) with single coronary arteries, 36 (24.8%) with ACAOS and an interarterial course, and 5 (3.5%) with coronary artery fistulas. The remaining 96 (66.2%) patients were classified as having benign variants. CONCLUSIONS The prevalence of CAA detected by CCTA is not negligible. Because of its noninvasive nature, relatively low cost and low radiation exposure, a further increase in the utilisation of CCTA may be expected, which may consequently be paralleled by an increasing absolute number of incidentally detected CAAs. Hence, awareness of the main issues and possible management strategies regarding CAAs is of importance for every treating physician.

DOI: <https://doi.org/10.4414/smwm.2016.14294>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-124274>

Journal Article

Published Version



The following work is licensed under a Creative Commons: Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.

Originally published at:

Gräni, Christoph; Benz, Dominik C; Schmied, Christian; Vontobel, Jan; Possner, Mathias; Clerc, Olivier F; Mikulicic, Fran; Stehli, Julia; Fuchs, Tobias A; Pazhenkottil, Aju P; Gaemperli, Oliver; Kaufmann, Philipp A; Buechel, Ronny Ralf (2016). Prevalence and characteristics of coronary artery anomalies detected by coronary computed tomography angiography in 5 634 consecutive patients in a single centre in Switzerland. *Swiss Medical Weekly*, 146:w14294.
DOI: <https://doi.org/10.4414/smww.2016.14294>

Prevalence and characteristics of coronary artery anomalies detected by coronary computed tomography angiography in 5634 consecutive patients in a single centre in Switzerland

Christoph Gräni^a*, Dominik C. Benz^a*, Christian Schmied^b, Jan Vontobel^a, Mathias Possner^a, Olivier F. Clerc^a, Fran Mikulicic^a, Julia Stehli^a, Tobias A. Fuchs^a, Aju P. Pazhenkottil^a, Oliver Gaemperli^{a,b}, Philipp A. Kaufmann^a, Ronny R. Buechel^a

^a Department of Nuclear Medicine, Cardiac Imaging, University Hospital Zurich, Switzerland

^b Department of Cardiology, University Hospital Zurich, Switzerland

* Christoph Gräni and Dominik C. Benz share first authorship

Summary

STUDY PRINCIPLES: Coronary computed tomography angiography (CCTA) allows three-dimensional visualisation of the origin, course and ending of the coronary vessels with high spatial resolution, yielding an accurate depiction of coronary artery anomalies (CAAs). This study sought to determine the prevalence, incidence and characteristics of CAAs detected with CCTA in a single centre in Switzerland.

METHODS: CAAs were retrospectively identified in 5634 consecutive patients referred for CCTA between March 2007 and July 2015. Single coronary arteries, Bland-White-Garland syndrome, anomalous coronary arteries originating from the opposite site of the sinus of Valsalva (ACAOS) with an interarterial course and coronary artery fistulas were classified as potentially malignant CAAs.

RESULTS: We identified 145 patients with CAAs, resulting in an overall prevalence of 2.6% and cumulative incidence of 2.1% in all patients referred for CCTA in the observation period. Forty-nine (33.8%) patients showed malignant CAAs including 1 (0.7%) patient with Bland-White-Garland syndrome, 7 (4.8%) with single coronary arteries, 36 (24.8%) with ACAOS and an interarterial course, and

5 (3.5%) with coronary artery fistulas. The remaining 96 (66.2%) patients were classified as having benign variants. **CONCLUSIONS:** The prevalence of CAA detected by CCTA is not negligible. Because of its noninvasive nature, relatively low cost and low radiation exposure, a further increase in the utilisation of CCTA may be expected, which may consequently be paralleled by an increasing absolute number of incidentally detected CAAs. Hence, awareness of the main issues and possible management strategies regarding CAAs is of importance for every treating physician.

Key words: coronary artery anomalies; coronary computed tomography angiography; CCTA; anomalous coronary artery originating from the opposite sinus of Valsalva; ACAOS

Introduction

The incidence of coronary artery anomalies (CAAs) in the general population is reported to be 0.3–5.6% [1, 2]. Coronary computed tomography angiography (CCTA) is considered the primary imaging modality to detect and characterise the anatomy of a CAA. It has a higher rate of detection of CAAs than invasive coronary angiography and other noninvasive imaging modalities, because three-dimensional visualisation of the entire coronary tree [3, 4] allows accurate depiction of the origin, course and ending of the coronary vessels [5].

CCTA has seen substantial technical advances over the last decade, particularly with regard to spatial resolution and an impressive reduction in radiation dose exposure [6]. Consequently, these developments were paralleled by a growing use of CCTA in clinical routine and increasing importance for noninvasive assessment of suspected coronary artery disease (CAD) in patients with low-to-intermediate pretest probability [7]. Thus, it may be expected that the incidental detection of CAAs will see a further increase, and referring

Abbreviations

ACAOS	anomalous coronary arteries originating from the opposite sinus of Valsalva
CAA	coronary artery anomaly
CAD	coronary artery disease
CCTA	coronary computed tomography angiography
LAD	left anterior descending coronary artery
LCS	left coronary sinus of Valsalva
LCX	left circumflex coronary artery
LM	left main stem
RIM	ramus intermedius artery
RCS	right coronary sinus of Valsalva
RCA	right coronary artery
SCD	sudden cardiac death

cardiologists and general physicians will be confronted to a greater extent with this entity.

Some CAAs, such as anomalous coronary arteries originating from the opposite site of the sinus of Valsalva (ACAOS), coronary artery fistulas or Bland-White-Garland syndrome are considered to be associated with adverse cardiac events [8–12]. ACAOS can be classified on the basis of the origin of the anomalous vessel and according to the anomalous vessel course as ACAOS with an interarterial, retroaortic or prepulmonic course (fig. 1). ACAOS, especially those with an interarterial course, are of particular interest as this anomaly is associated with ventricular arrhythmia, syncope and sudden cardiac death (SCD) [9, 13–15]. In fact, ACAOS have been demonstrated to constitute the underlying cause of SCD in up to 20% in young athletes and in up to 30% in military recruits [13, 16, 17]. This study sought to determine the prevalence, incidence and characteristics of CAA detected with CCTA in a single centre in Switzerland.

Methods

Patients and anatomy

All 5634 consecutive patients undergoing CCTA at our institution between March 2007 and July 2015 were retrospectively reviewed for CAA. Classification of CAAs was made based on anatomical and functional characteristics. Anatomical characteristics were assessed as follows: CAAs were defined as a coronary artery with abnormal origin,

course, termination or anomalies of intrinsic coronary arterial anatomy [1]. Myocardial bridging (i.e., an anomalous course of the coronary artery partially within the myocardial muscle tissue) is considered to be a normal variant [18, 19] and was therefore not included in the present study. Coronary artery ectasia is defined as an arterial segment with a diameter 1.5 times that of the normal adjacent artery segment. In patients with CAD, coronary artery ectasia, a form of abnormal intrinsic coronary arterial anatomy is considered to be a CAD correlate. Therefore, we classified coronary artery ectasia as a CAA only in patients without concomitant obstructive CAD. Obstructive CAD was defined as $\geq 50\%$ luminal diameter narrowing as demonstrated by CCTA. In patients with ectasia, associated underlying diseases were assessed. As single coronary arteries, Bland-White-Garland syndrome, ACAOS with an interarterial course and coronary artery fistulas are associated with adverse cardiac events, we further classified these, based on functional characteristics with possible haemodynamic relevance as potentially “malignant CAAs”. All other CAAs were considered as benign variants.

CCTA Imaging

CCTA was performed on 64-slice (LightSpeed VCT XT, Discovery 750 HD) and 256-slice (Revolution CT; all GE Healthcare, Waukesha, WI, USA) CT scanners using prospective electrocardiographic triggering with the smallest possible x-ray window at 75% of the R-R cycle, according to current guidelines and as previously described [20, 21]. Prior to examination all patients received 2.5 mg isosorbide-dinitrate sublingually (Isoket, Schwarz Pharma, Monheim, Germany) and up to 30 mg metoprolol (Beloc Zok, AstraZeneca, London, UK) was administered intravenously if the heart rate was >65 per minute in order to obtain optimal image quality [20]. Iodixanol (Visipaque 320, 320 mg/ml, GE Healthcare) was injected into an antecubital vein followed by 50 ml saline solution. Volume and flow rate were adapted to body surface area [22]. All images were transferred to an external workstation (AW 4.4, GE Healthcare) for image reconstruction and evaluation. Curved multiplanar reconstructions and three-dimensional volume rendering techniques were performed for analysis. Values for effective radiation dose were estimated for CCTA as the product of the dose length product (DLP) times a conversion coefficient for the chest ($k = 0.014 \text{ mSv/(mGy} \times \text{cm)}$) as previously described [23, 24].

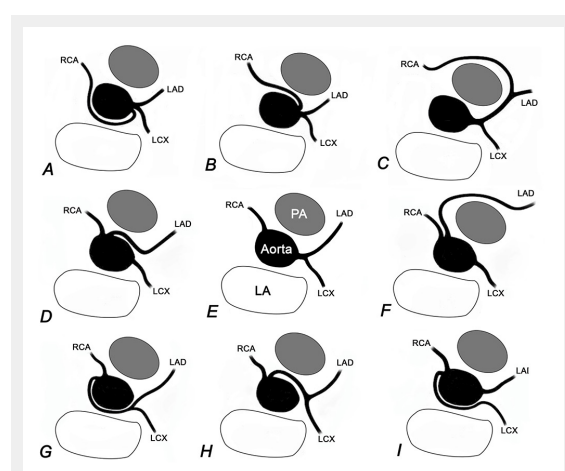


Figure 1

Schematic illustration of a selection of coronary artery anomalies. For comparison, the normal anatomical situs is given in the middle (i.e., Panel E). A: ACAOS with RCA originating from the LCS with a retroaortic course. B: ACAOS with RCA originating from the LCS with an interarterial course. C: “Single left” coronary artery with a RCA originating from the LAD and a prepulmonic course. D: ACAOS with LAD originating from the RCS with an interarterial course. F: ACAOS with LAD originating from the RCS with a prepulmonic course. G: ACAOS with LM originating from the RCS with a retroaortic course. H: ACAOS with LM originating from the RCS with an interarterial course. I: ACAOS with LCX originating from the RCS with a retroaortic course.

ACAOS = anomalous coronary arteries originating from the opposite sinus of Valsalva; LAD = left anterior descending artery; LCS = left coronary sinus; LCX = left circumflex coronary artery; LM = left main stem; RCA = right coronary artery; RCS = right coronary sinus;

Statistical analysis

All statistical analyses were performed using SPSS Statistics 22 (IBM Corporation, Armonk, NY). Data are reported as median \pm interquartile range (IQR, 25th–75th percentile), or mean \pm standard deviation (SD), or percentages for nonparametric and parametric data, respectively. Continuous variables were analysed using the Student’s t-test or Mann-Whitney U-test, where appropriate. Categorical data were analysed with chi-squared test or Fisher’s exact test. A p-value <0.05 was considered statistically significant. Overall prevalence of CAA was calculated as the proportion of patients with CAA out of all patients undergoing CCTA during the observation period. Cumulative incidence was calculated as the proportion of patients with newly

diagnosed CAA out of all patients undergoing CCTA during the observation period.

Ethics

The study was approved by the local ethics committee and the need for written informed consent was waived. KEK-ZH-Nr. 2015-0235.

Results

We identified 145 patients with CAA and an overall prevalence of 2.6%. CAA classified by vessel origination, course and termination and its prevalence are shown in table 1. Baseline characteristics of malignant and benign CAAs are given in table 2. CAA was newly diagnosed in 117 (80.1%) of patients with a cumulative incidence of 2.1% in the observation period. Out of these, 12 patients were referred for CCTA specifically for exclusion of CAA owing to a suspect finding for CAA e.g. in echocardiography. All other patients were referred for CAD exclusion. Thus, CAA was an incidental finding in the remaining

105 (72.4%) patients. Forty-nine (33.8%) patients showed malignant CAAs including 1 (0.7%) patient with Bland-White-Garland syndrome, 7 (4.8%) with single coronary arteries (fig. 2), 36 (24.8%) with ACAOS and an interarterial course (fig. 3), and 5 (3.5%) with coronary artery fistulas (fig. 4). The remaining 96 (66.2%) patients were classified as having benign coronary variants. Of note, typical angina was significantly more frequent ($p = 0.006$) in patients with potentially malignant CAA than in patients with benign variants. Twelve (8.3%) patients showed ectasia of the coronary arteries and out of these, six (50.0%) had concomitant dilated arteriopathy of the ascending or descending aorta (including one patient with known Kawasaki syndrome and one patient with Marfan syndrome). Median effective radiation dose of CCTA was 1.4 mSv (IQR 1.2–2.3).

Discussion

This is the largest study assessing the prevalence, incidence and characteristics of CAA detected by means of CCTA in

Table 1: Classification of coronary artery anomalies.

		Cases, n	Cases, %	Prevalence, %
Anomalies of vessel origin and course (n = 107)	Separate ostia for LAD and LCX	27	18.6	0.48
	Single coronary artery*	7		0.12
	Single right coronary artery	6	4.1	0.11
	Single left coronary artery	1	0.7	0.02
	Absent LCX	2	1.4	0.04
	Bland-White-Garland syndrome*	1	0.7	0.02
	High take off LAD	1	0.7	0.02
	High take off RCA	3	2.1	0.05
	ACAOS	66		1.17
	ACAOS with interarterial course*	36		0.64
	ACAOS with prepulmonic course	3		0.05
	ACAOS with retroaortic course	27		0.37
	RCA of LCS	33	22.8	0.59
	LAD of RCS	2	1.4	0.04
	LCX of RCS	10	6.9	0.18
	LAD and LCX of RCS	2	1.4	0.04
	LAD of RCA	2	1.4	0.04
	LCX of RCA	11	7.6	0.20
	LM from non-coronary sinus	5	3.4	0.09
	RCA from non-coronary sinus	1	0.7	0.02
Anomalies of intrinsic coronary arterial anatomy (n = 33)	Duplication of LAD	6	4.1	0.11
	Duplication of RIM	2	1.4	0.04
	Duplication of RCA	1	0.7	0.02
	Ectasia	12	8.3	0.21
	Hypoplasia of LCX	8	5.5	0.14
	Hypoplasia of RCA	4	2.8	0.07
Anomalies of vessel termination (n = 5)	Coronary artery fistula*	5		0.09
	LAD to pulmonary artery	3	2.1	0.05
	LAD and RCA to pulmonary artery	1	0.7	0.02
	LCX to coronary sinus	1	0.7	0.02

ACAOS = anomalous coronary artery originating from the opposite sinus of Valsalva; LAD = left anterior descending coronary artery; LCS = left coronary sinus of Valsalva; LCX = left circumflex coronary artery; LM = Left main stem; RCA = right coronary artery; RCS = Right coronary sinus of Valsalva; RIM = Ramus intermedius artery

* malignant coronary artery anomaly

a population referred for CCTA in Switzerland. The overall prevalence of CAA (i.e., 2.6%) in the observation period detected with CCTA is comparable to that in previous studies [1, 2, 12, 25]. A recent smaller study from our institution showed a higher prevalence of CAA (i.e., 7.9%) depicted with CCTA. This difference may be explained by the fact that myocardial bridging (prevalence 3.4%) was included in this study, contrary to the present work where myocardial bridging was not classified as a true coronary anomaly but rather as a normal variant owing to its common occurrence [26]. The most commonly found CAA in our study was ACAOS. In line with previous studies, among the ACAOS variants a right coronary artery (RCA) arising from the left coronary sinus (LCS) were most frequently represented in our population [27, 28]. In a study analysing 126 595 patients undergoing invasive coronary arteriography over a 28-year period, the rate of RCA originating from LCS was six times higher than the rate of

left coronary artery originating from the right coronary sinus (RCS) (0.17% versus 0.047%) [28]. By contrast, we observed a similar proportion of the two ACAOS variants (i.e., 0.59% versus 0.46%). This may be in part a result of the better performance of CCTA over invasive coronary angiography, particularly for the detection and characterisation of patients with a left coronary artery originating from the RCS [27, 28].

Imaging modalities

Whenever knowledge of the anatomy of the cardiac vessels is crucial, CCTA represents a highly valuable noninvasive modality because of its capability to visualise the coronary

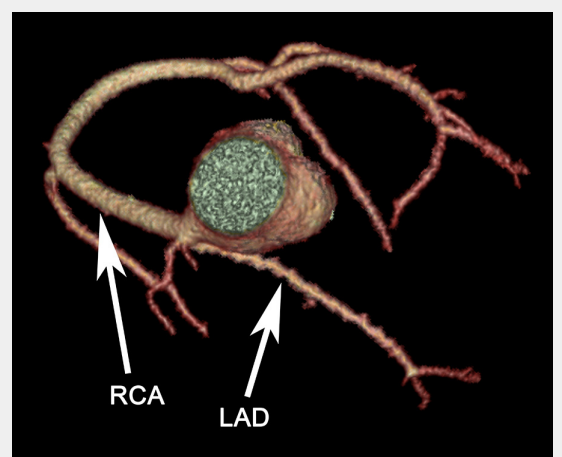


Figure 2
A patient with suspected coronary artery anomaly in echocardiography has a “single right” coronary artery, as depicted by CCTA.
CCTA = coronary computed tomography angiography; LAD = left anterior descending artery; RCA = right coronary artery

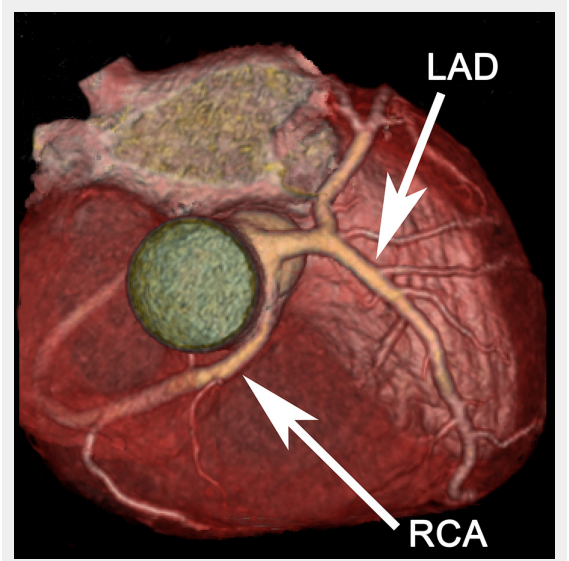


Figure 3
Incidental finding of an ACAOS variant with RCA originating from LCS and a malignant interarterial course of the vessel in a patient referred for CCTA for exclusion of CAD.
ACAOS = anomalous coronary arteries originating from the opposite sinus Valsalva; CAD = coronary artery disease; CCTA = coronary computed tomography angiography; LAD = left anterior descending artery; LCS = left coronary sinus; RCA = right coronary artery

Table 2: Patient characteristics.			
Characteristic	Malignant CAA n = 49	Benign CAA n = 96	p-value
Male gender, n (%)	36 (73%)	69 (72%)	NS
Age (years), mean ± SD	53 ± 14	57 ± 14	NS
Cardiovascular risk factors, n (%)			
Obesity (BMI ≥30 kg/m ²)	12 (24%)	22 (22%)	NS
Smoking	17 (35%)	29 (30%)	NS
Diabetes mellitus	5 (10.2%)	7 (7%)	NS
Hypertension	17 (35%)	45 (47%)	NS
Dyslipidaemia	15 (31%)	29 (30.0%)	NS
Positive family history for CAD	13 (27%)	22 (23%)	NS
Clinical symptoms, n (%)			
Asymptomatic	14 (29%)	32 (33%)	NS
Typical angina	15 (31%)	11 (12%)	0.006
Atypical angina	9 (18%)	26 (27%)	NS
Dyspnoea	1 (2%)	12 (13%)	NS
Palpitations	8 (16%)	10 (10%)	NS
Vertigo	0	1 (1%)	NS
Syncope	2 (4%)	4 (4%)	NS

BMI = body mass index; CAA = coronary artery anomaly; CAD = coronary artery disease; NS = not significant; SD = standard deviation

arteries accurately and three-dimensionally, yielding a higher detection rate over invasive coronary angiography [26]. Regarding echocardiography, reported data suggest that transoesophageal echocardiography is more sensitive than transthoracic echocardiography in identifying CAA. This is mainly driven by an increased sensitivity for assessing the vessel course. However, it remains a semi-invasive technique (it involves insertion of a tube into the oesophagus and sedation) characterised by a significant level of operator dependence. Finally, both echocardiography tech-

niques and cardiac magnetic resonance imaging are able to accurately assess only the proximal tract of the coronary arteries and, therefore, their diagnostic capabilities are limited to only a small part of the coronary artery anatomy [4, 29].

Benign variants of CAA

An absent left main stem (with separate ostia for the left anterior descending [LAD] and left circumflex [LCX] arteries, fig. 5) was present second most frequently (i.e., in 18.6%). Of note, certain authors suggest that separate ostia for the LAD and LCX is rather a normal variant than an anomaly with little clinical significance [1]; however, recognising this condition before coronary bypass surgery may be crucial. Also, in cases of difficulty in cannulating the LAD or LCX in invasive coronary angiography, CCTA serves as an ideal backup imaging modality. This is of particular interest as CCTA seemed also to outperform invasive coronary angiography in proximal segment evaluation of the coronary arteries [26] and helps to differentiate between absence of the left main stem and LAD, or occluded or hypoplastic LCX occlusion [30].

Malignant variants of CAA

A high proportion (i.e., 33.8%) of CAAs, including Bland-White-Garland syndrome, single coronary artery, ACAOS with an interarterial course and fistulas were considered as potentially malignant variants because of their potentially haemodynamic clinical relevance [31]. Previous studies reported that approximately 20% of CAAs are clinically relevant and carry an increased risk of myocardial infarction, malignant ventricular arrhythmia, congestive heart failure, syncope and SCD [8–12, 28]. Congruently with previous reports, typical angina was significantly more frequently reported in conjunction with a potentially malignant CAA in our cohort [25, 32–35]. Owing to a lack of clear guideline recommendations, the management of patients with CAAs remains fraught with uncertainty. This is particularly true for asymptomatic individuals with coincidentally discovered CAAs. It has been recommended that, in patients with Bland-White-Garland syndrome or ACAOS with origin of the left coronary artery from the right sinus and ACAOS who survived SCD, showed serious ventricular tachyarrhythmias or documented myocardial ischaemia, surgical treatment represents first-line therapy [11]. Further risk stratification with single photon emission computed tomography myocardial perfusion imaging (SPECT-MPI), positron emission tomography myocardial perfusion imaging (PET-MPI) or stress echocardiography may be warranted in unclear cases [36–38]. As a slit-like ostium, intramural course and proximal narrowing of the anomalous vessel are believed to confer a higher risk for adverse cardiac events, exact anatomic depiction as offered by CCTA may be helpful for further risk stratification [8, 9, 13–15, 39–42]. Furthermore, age, sex and physical activity should be incorporated in the risk stratification as well, since there is evidence that especially young (<30 years) male athletes or military recruits are at increased risk for SCD [43], whereas in older patients the risk seems to be rather negligible [44]. Surgical revascularisation may consist of ectopic coronary reimplantation, creation of a new ostium at

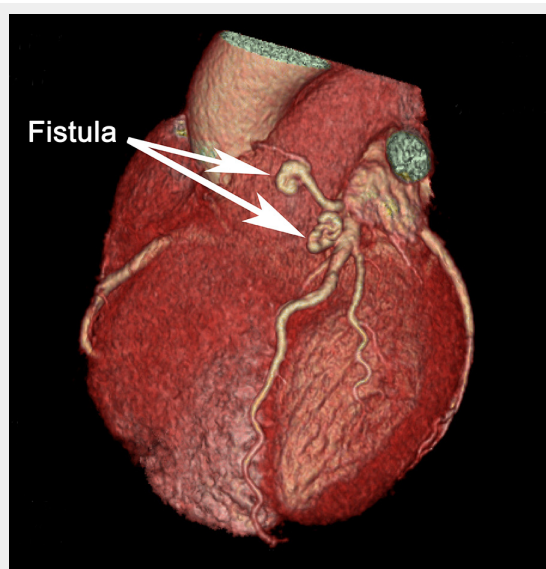


Figure 4

CCTA of a 64-year-old patient with atypical angina referred for exclusion of CAD shows no relevant CAD but a coronary artery fistula originating from the LAD and terminating in the pulmonary artery, potentially causing his symptoms.

CAD = coronary artery disease; CCTA = coronary computed tomography angiography; LAD = left anterior descending artery

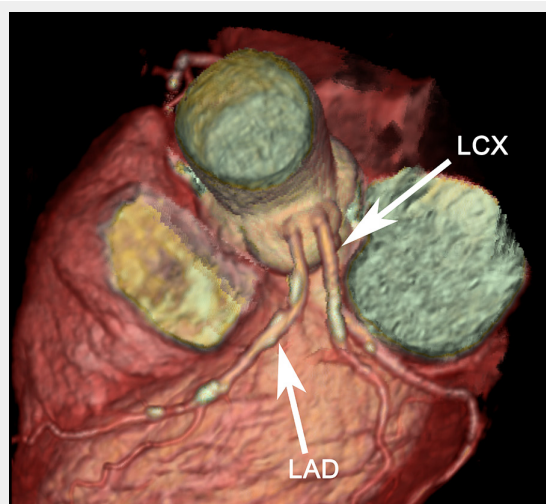


Figure 5

CCTA of a 63-year-old male shows obstructive CAD and absent left main stem with separate ostium for LAD and LCX. Absent left main stem is considered a benign variant of CAA, but the finding may be of clinical importance for eventual revascularisation procedures. CAA = coronary artery anomaly; CAD = coronary artery disease; CCTA = coronary computed tomography angiography; LAD = left anterior descending artery; LCX = left circumflex coronary artery

the end of the ectopic artery intramural segment (so-called unroofing procedure), or coronary bypass grafting [43]. Of note, there are no controlled studies that have evaluated the outcome of intervention in asymptomatic individuals.

Coronary arterial fistula is a rare anomaly in which a communication is present between a coronary artery and a cardiac chamber or another vascular structure. Even in small coronary artery fistulas, a “steal-phenomenon” caused by redirection of saturated blood away from the myocardium may cause hypoperfusion and reduction of myocardial blood flow distally of the supplying coronary artery. Haemodynamically insignificant fistulas, which are clinically silent and not associated with other abnormal findings, may not require further treatment. However, haemodynamically significant fistulas should be closed by ligation or coiling [11]. Similarly, a “steal-phenomenon” caused by reversed flow in the coronary artery into a pulmonary artery as a result of decreased pulmonary artery pressure after birth may be present in Bland-White-Garland syndrome patients [45]. International guidelines suggest that in adults with previously unrecognised Bland-White-Garland syndrome and reduced systolic function, surgical myocardial revascularisation should be performed in order to achieve a dual coronary supply [11].

Although coronary artery ectasia is not a typical malignant CAA, it carries an increased risk of myocardial infarction due to vasospasm, slower coronary blood flow and thrombosis, typically within the dilated segments. Coronary artery ectasia was present third most frequently (i.e., in 8.3%). Beside CAD-related ectasia, which was not included in the present study, the most common underlying cause of ectasia is associated with small-, medium- and large-vessel vasculitis and sickle cell disease [46, 47]. In our study, 50% of patients with coronary artery ectasia showed concomitant dilated arteriopathy, which is in concordance with Papadakis et al., who reported a similarly high coincidence of coronary ectasia in patients with ascending aortic aneurysm [48]. Due to a lack of studies and guidelines, management recommendations for coronary artery ectasia are solely based on personal experiences. Therapy should be tailored to each individual case after assessment of severity, history of complications, underlying aetiology, and comorbidities [47]. However, data on optimal treatment strategies (i.e., surgical versus conservative treatment) are scarce and to some extent controversial, rendering patient management challenging, mainly because of the fact that CAAs are rare, their anatomical spectrum is diverse, and the age of first clinical presentation may vary substantially. Thus, assessment of coronary artery anatomy by CCTA plays a central role in management of these entities, especially in CAAs with high risk anatomic features potentially conferring hemodynamic relevance [49, 50].

Limitations

CAAs represent a wide group of congenital disorders whose pathophysiological mechanisms and clinical consequences are highly variable. Some experts proposed to categorise CAAs based on functional characteristics as major, minor, haemodynamically relevant and severe versus non-severe CAAs. We are aware that the term potentially “malignant CAA” is an imperfect compromise. Furthermore, in

the current study, ACAOS were not analysed according to other high-risk anatomical features such as intramural (in the aortic wall) course, slit-like ostium and proximal narrowing [42, 51] and therefore misclassification may be possible in certain ACAOS variants.

There is evidence that in very rare cases myocardial bridging (i.e., an anomalous course of the coronary artery partially within the myocardial muscle tissue) is associated with adverse cardiac events [52] and, historically, myocardial bridging was classified as a CAA. However, myocardial bridging is quite common and is found in up to 86% of all autopsies. Thus, the entity of myocardial bridging should rather be considered as a normal variant [18, 19] and we excluded these patients from our study. Finally, it may be perceived as a limitation of the present study that there is no control group, such as a cohort where the coronary anomalies were detected by invasive coronary angiography. As all patients were referred because of suspected CAD (owing to symptoms or high cardiovascular risk) or for CAA exclusion, the prevalence of CAA in our population may be higher than in a general population as a result of selection bias. Thus, extrapolation of the results of this study to a general population should be made only with caution.

Conclusion

The prevalence of CAA detected by CCTA in Switzerland is not negligible. Exact anatomic characterisation of CAA is essential for identifying potentially malignant characteristics and guiding further work-up and treatment decisions. Because of its noninvasive nature, relatively low cost and low radiation exposure, a further increase of the utilisation of CCTA may be expected, which may consequently be paralleled by an increasing absolute number of incidentally detected CAAs. Hence, awareness of the main issues and possible management strategies regarding CAAs is of importance for every treating physician.

Disclosure statement: The University Hospital Zurich holds a research contract with GE Healthcare.

Correspondence: Ronny R. Buechel, MD, Cardiac Imaging, Department of Nuclear Medicine, University Hospital Zurich, Ramistrasse 100, CH-8091 Zurich, ronny.buechel@atjusz.ch

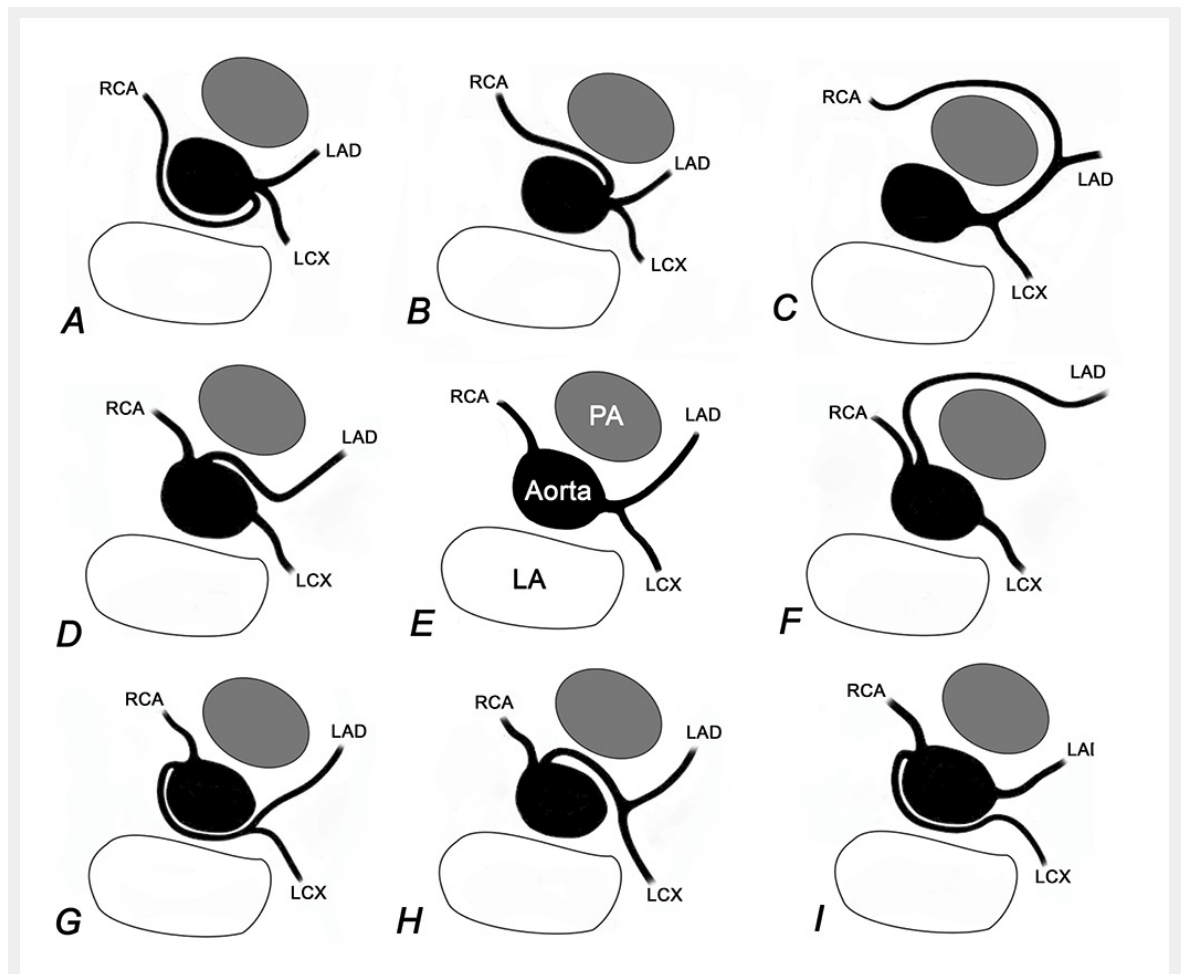
References

- 1 Angelini P. Coronary artery anomalies: an entity in search of an identity. *Circulation*. 2007;115(10):1296–305.
- 2 Kim SY, Seo JB, Do KH, Heo JN, Lee JS, Song JW, et al. Coronary artery anomalies: classification and ECG-gated multi-detector row CT findings with angiographic correlation. *Radiographics*. 2006;26(2):317–33; discussion 333–4.
- 3 Kang JW, Seo J, Chae E, Jang Y, Do KH, Lee J, et al. Coronary Artery Anomalies: Classification and Electrocardiogram-Gated Multidetector Computed Tomographic Findings. *Semin Ultrasound CT MRI*. 2008;29(3):182–94.
- 4 Zeina AR, Blinder J, Sharif D, Rosenschein U, Barneir E. Congenital coronary artery anomalies in adults: non-invasive assessment with multidetector CT. *Br J Radiol*. 2009;82(975):254–61.

- 5 Angelini P, Flamm SD. Newer concepts for imaging anomalous aortic origin of the coronary arteries in adults. *Catheter Cardiovasc Interv.* 2007;69(7):942–54.
- 6 Fuchs TA, Stehli J, Bull S, Dougoud S, Clerc OF, Herzog BA, et al. Coronary computed tomography angiography with model-based iterative reconstruction using a radiation exposure similar to chest X-ray examination. *Eur Heart J.* 2014;35(17):1131–6.
- 7 Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease The Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J.* 2013;34(38):2949–3003.
- 8 Camarda J, Berger S. Coronary artery abnormalities and sudden cardiac death. *Pediatr Cardiol.* 2012;33(3):434–8.
- 9 Frommelt PC. Congenital coronary artery abnormalities predisposing to sudden cardiac death. *Pacing Clin Electrophysiol.* 2009;32(Suppl 2):S63–6.
- 10 Seon HJ, Kim YH, Choi S, Kim KH. Complex coronary artery fistulas in adults: evaluation with multidetector computed tomography. *Int J Cardiovasc Imaging.* 2010;26(Suppl 2):261–71.
- 11 Warnes C, Williams R, Bashore T, Child J, Connolly H, Dearani J, et al. ACC/AHA 2008 Guidelines for the Management of Adults With Congenital Heart Disease A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease): Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation.* 2008;118(23):e714–833.
- 12 Loukas M, Germain A, Gabriel A, John A, Tubbs S, Spicer D. Coronary artery fistula: a review. *Cardiovasc Pathol.* 2015;24(3):141–8.
- 13 Lorenz EC, Mookadam F, Mookadam M, Moustafa S, Zehr KJ. A systematic overview of anomalous coronary anatomy and an examination of the association with sudden cardiac death. *Rev Cardiovasc Med.* 2006;7(4):205–13.
- 14 Harmon KG, Drezner JA, Maleszewski JJ, Lopez-Anderson M, Owens D, Prutkin JM, et al. Pathogenesis of sudden cardiac death in national collegiate athletic association athletes. *Circ Arrhythm Electrophysiol.* 2014;7(2):198–204.
- 15 Maron B, Doerer J, Haas T, Tierney D, Mueller F. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. *Circulation.* 2009;119(8):1085–92.
- 16 Basso C, Maron B, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol.* 1999;35(6).
- 17 Eckart R, Scoville S, Campbell C, Shry E, Stajduhar K, Potter R, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med.* 2004;141(11):829–34.
- 18 Lazoura O, Kanavou T, Vassiou K, Gkiokas S, Fezoulidis IV. Myocardial bridging evaluated with 128-multi detector computed tomography coronary angiography. *Surg Radiol Anat.* 2010;32(1):45–50.
- 19 Konen E, Goitein O, Segni E. Myocardial bridging, a common anatomical variant rather than a congenital anomaly. *Semin Ultrasound CT MR.* 2008;29(3):195–203.
- 20 Buechel RR, Husmann L, Herzog BA, Pazhenkottil AP, Nkoulou R, Ghadri JR, et al. Low-dose computed tomography coronary angiography with prospective electrocardiogram triggering: feasibility in a large population. *J Am Coll Cardiol.* 2011;57(3):332–6.
- 21 Abbara S, Arbab-Zadeh A, Callister T, Desai M, Mamuya W, Thomson L, et al. SCCT guidelines for performance of coronary computed tomographic angiography: A report of the Society of Cardiovascular Computed Tomography Guidelines Committee. *J Cardiovasc Comput Tomogr.* 2009;3(3):190–204.
- 22 Pazhenkottil A, Husmann L, Buechel R, Herzog B, Nkoulou R, Burger I, et al. Validation of a new contrast material protocol adapted to body surface area for optimized low-dose CT coronary angiography with prospective ECG-triggering. *Int J Cardiovasc Imaging.* 2010;26(5):591–7.
- 23 Einstein A, Moser K, Thompson R, Cerqueira M, Henzlova M. Radiation dose to patients from cardiac diagnostic imaging. *Circulation.* 2007;116(11):1290–305.
- 24 Hausleiter J, Meyer T, Hermann F, Hadamitzky M, Krebs M, Gerber T, et al. Estimated Radiation Dose Associated With Cardiac CT Angiography. *JAMA.* 2009;301(5):500–7.
- 25 Yau J, Singh R, Halpern E, Fischman D. Anomalous Origin of the Left Coronary Artery From the Pulmonary Artery in Adults: A Comprehensive Review of 151 Adult Cases and A New Diagnosis in a 53-Year-Old Woman. *Clin Cardiol.* 2011;34(4):204–10.
- 26 Ghadri JR, Kazakauskaitė E, Braunschweig S, Burger IA, Frank M, Fiechter M, et al. Congenital coronary anomalies detected by coronary computed tomography compared to invasive coronary angiography. *BMC Cardiovasc Disord.* 2014;14:81.
- 27 Malagò R, D'Onofrio M, Brunelli S, La Grutta L, Midiri M, Tavella D, et al. Anatomical variants and anomalies of the coronary tree studied with MDCT coronary angiography. *Radiol Med.* 2010;115(5):679–92.
- 28 Yamanaka O, Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary arteriography. *Cathet Cardiovasc Diagn.* 1990;21(1):28–40.
- 29 Fernandes F, Alam M, Smith S, Khaja F. The role of transesophageal echocardiography in identifying anomalous coronary arteries. *Circulation.* 1993;88(6):2532–40.
- 30 Hacıoglu Y, Budoff M. Is the left anterior descending artery really absent? – A decisive input from coronary CT angiography. *Catheter Cardiovasc Interv.* 2010;76(1):117–20.
- 31 Erol C, Seker M. Coronary artery anomalies: the prevalence of origin, course, and termination anomalies of coronary arteries detected by 64-detector computed tomography coronary angiography. *J Comput Assist Tomogr.* 2011;35(5):618–24.
- 32 Kimbiris, Iskandrian, Segal, Bemis. Anomalous aortic origin of coronary arteries. *Circulation.* 1978;58(4):606–15.
- 33 Koneru J, Samuel A, Joshi M, Hamden A, Shamoone FE, Bikkina M. Coronary anomaly and coronary artery fistula as cause of angina pectoris with literature review. *Case Rep Vasc Med.* 2011;486187.
- 34 Prachar, Muzika, Dittel, Kubiena. Angina pectoris bei Koronar-anomalie. *Dtsch Med Wochenschr.* 1991;116(13):496–8.
- 35 Trost B, Halperin J. Unstable angina in a patient with anomalous origin of the left main coronary artery from the right sinus of Valsalva. *Reviews in cardiovascular medicine.* 2010;11(2):112–6.
- 36 Uebles C, Groebner M, von Ziegler F, Becker A, Rischpler C, Tegtmeyer R, et al. Combined anatomical and functional imaging using coronary CT angiography and myocardial perfusion SPECT in symptomatic adults with abnormal origin of a coronary artery. *Int J Cardiovasc Imaging.* 2012;28(7):1763–74.
- 37 De Luca L, Bovenzi F, Rubini D, Niccoli-Asabella A, Rubini G, De Luca I. Stress-rest myocardial perfusion SPECT for functional assessment of coronary arteries with anomalous origin or course. *J Nucl Med.* 2004;45(4):532–6.
- 38 Ercin E, Gämperli O, Kaufmann P, Eberli FR. Bland-White-Garland syndrome: extensive collaterals prevent ischaemia. *Eur Heart J.* 2007;28(14):1672.
- 39 Jo Y, Uranaka Y, Iwaki H, Matsumoto J, Koura T, Negishi K. Sudden cardiac arrest: associated with anomalous origin of the right coronary artery from the left main coronary artery. *Tex Heart Inst J.* 2011;38(5):539–43.
- 40 Hill SF, Sheppard MN. A silent cause of sudden cardiac death especially in sport: congenital coronary artery anomalies. *Br J Sports Med.* 2014;48(15):1151–6.
- 41 Bria S, Chessa M, Abella R, Frigiola A, Bianco M, Palmieri V, et al. Aborted sudden death in a young football player due to anomalous origin of the left coronary artery: successful surgical correction. *Journal of cardiovascular medicine (Hagerstown, Md).* 2008;9(8):834–8.
- 42 Ashrafpoor G, Danchin N, Houyel L, Ramadan R, Belli E, Paul J-F. Anatomical criteria of malignancy by computed tomography angiography in patients with anomalous coronary arteries with an interarterial course. *Euro Radiol.* 2014;25(3):760–6.

- 43 Peñalver JM, Mosca RS, Weitz D, Phoon CK. Anomalous aortic origin of coronary arteries from the opposite sinus: a critical appraisal of risk. *BMC Cardiovasc Disord.* 2012;12:83.
- 44 Krasuski RA, Magyar D, Hart S, Kalahasti V, Lorber R, Hobbs R, et al. Long-term outcome and impact of surgery on adults with coronary arteries originating from the opposite coronary cusp. *Circulation.* 2011;123(2):154–62.
- 45 Katsuragi, Yamamoto, Tashiro, Nishihara, Toudou. Thallium-201 myocardial SPECT in Bland-White-Garland syndrome: two adult patients with inferoposterior perfusion defect. *J Nucl Med.* 1993;34(12):2182–4.
- 46 Pursnani A, Jacobs JE, Saremi F, Levisman J, Makaryus AN, Capuñay C, et al. Coronary CTA assessment of coronary anomalies. *J Cardiovasc Comput Tomogr.* 2012;6(1):48–59.
- 47 Dahhan A. Coronary artery ectasia in atherosclerotic coronary artery disease, inflammatory disorders, and sickle cell disease. *Cardiovasc Ther.* 2015;33(2):79–88.
- 48 Papadakis M, Leontiadis E, Manginas A, Voudris V, Pavlides G, Karatasakis G, et al. Frequency of coronary artery ectasia in patients undergoing surgery for ascending aortic aneurysms. *Am J Cardiol.* 2004;94(11):1433–5.
- 49 Shinbane JS, Shriki J, Fleischman F, Hindoyan A, Withey J, Lee C, et al. Anomalous coronary arteries: cardiovascular computed tomographic angiography for surgical decisions and planning. *World J Pediatr Congenit Heart Surg.* 2013;4(2):142–54.
- 50 Erol C, Seker M. The prevalence of coronary artery variations on coronary computed tomography angiography. *Acta Radiol.* 2012;53(3):278–84.
- 51 Angelini P. Letter by Angelini regarding article, “long-term outcome and impact of surgery on adults with coronary arteries originating from the opposite coronary cusp”. *Circulation.* 2011;124(14):e383.
- 52 Zhu CG, Liu J, Liu WD, Xu YL, Wu NQ, Guo YL, et al. Myocardial infarction caused by myocardial bridging in a male adolescent athlete. *J Cardiovasc Med (Hagerstown).* 2012;13(2):138–40.

Figures (large format)

**Figure 1**

Schematic illustration of a selection of coronary artery anomalies. For comparison, the normal anatomical situs is given in the middle (i.e., Panel E). A: ACAOS with RCA originating from the LCS with a retroaortic course. B: ACAOS with RCA originating from the LCS with an interarterial course. C: "Single left" coronary artery with a RCA originating from the LAD and a prepulmonic course. D: ACAOS with LAD originating from the RCS with an interarterial course. F: ACAOS with LAD originating from the RCS with a prepulmonic course. G: ACAOS with LM originating from the RCS with a retroaortic course. H: ACAOS with LM originating from the RCS with an interarterial course. I: ACAOS with LCX originating from the RCS with a retroaortic course.

ACAOS = anomalous coronary arteries originating from the opposite sinus of Valsalva; LAD = left anterior descending artery; LCS = left coronary sinus; LCX = left circumflex coronary artery; LM = left main stem; RCA = right coronary artery; RCS = right coronary sinus;

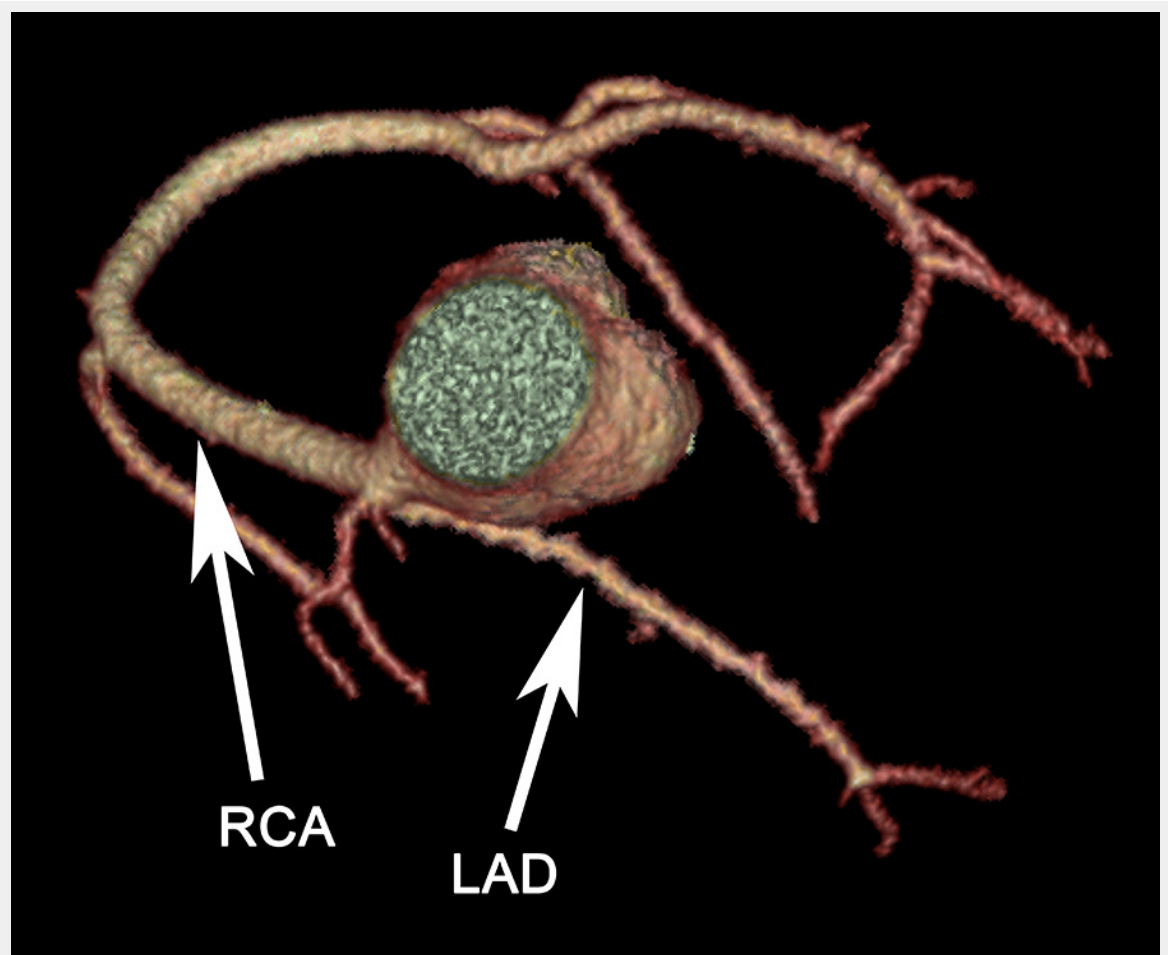


Figure 2

A patient with suspected coronary artery anomaly in echocardiography has a "single right" coronary artery, as depicted by CCTA. CCTA = coronary computed tomography angiography; LAD = left anterior descending artery; RCA = right coronary artery

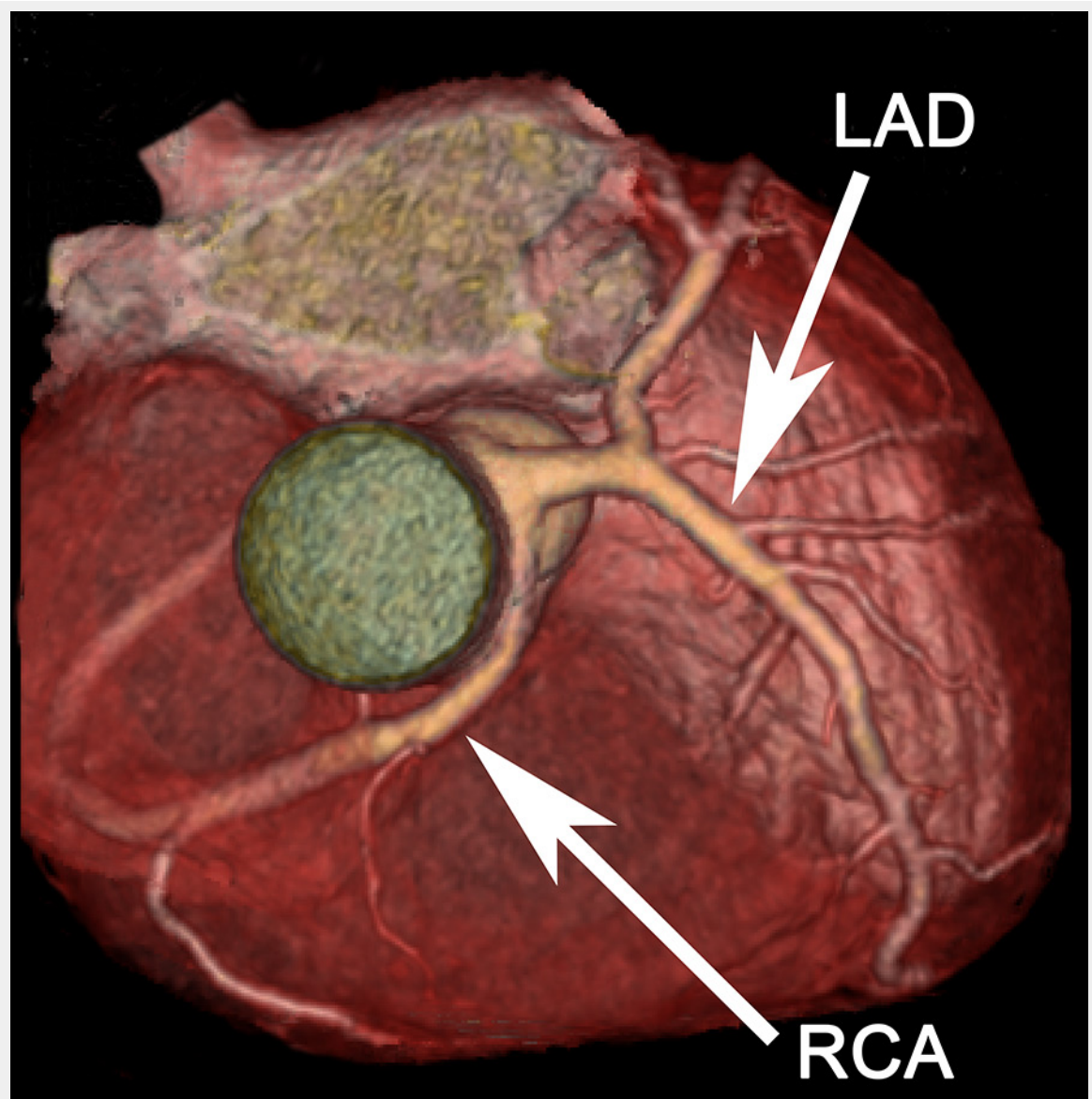


Figure 3

Incidental finding of an ACAOS variant with RCA originating from LCS and a malignant interarterial course of the vessel in a patient referred for CCTA for exclusion of CAD.

ACAOS = anomalous coronary arteries originating from the opposite sinus Valsalva; CAD = coronary artery disease; CCTA = coronary computed tomography angiography; LAD = left anterior descending artery; LCS = left coronary sinus; RCA = right coronary artery

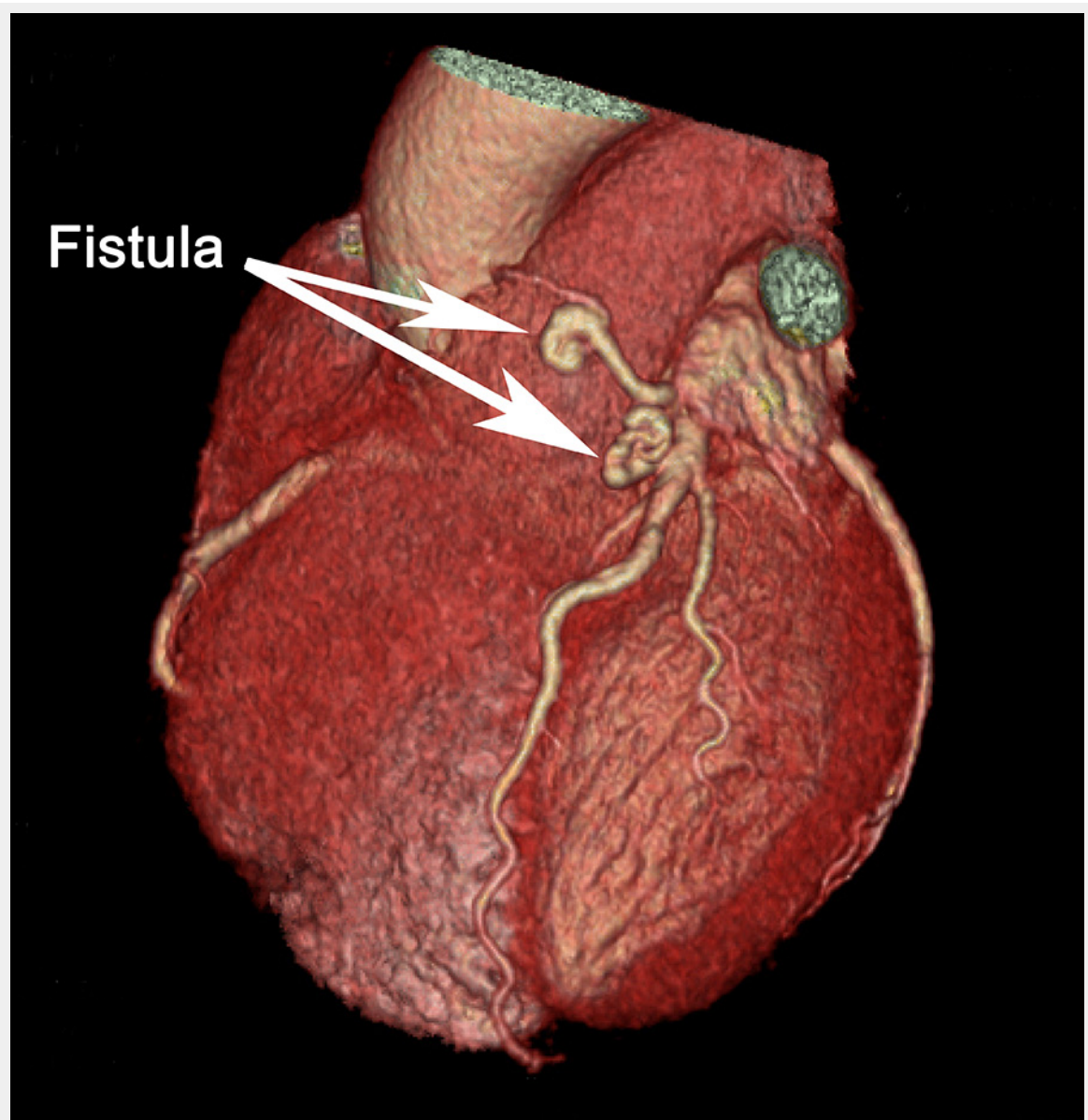


Figure 4

CCTA of a 64-year-old patient with atypical angina referred for exclusion of CAD shows no relevant CAD but a coronary artery fistula originating from the LAD and terminating in the pulmonary artery, potentially causing his symptoms.

CAD = coronary artery disease; CCTA = coronary computed tomography angiography; LAD = left anterior descending artery

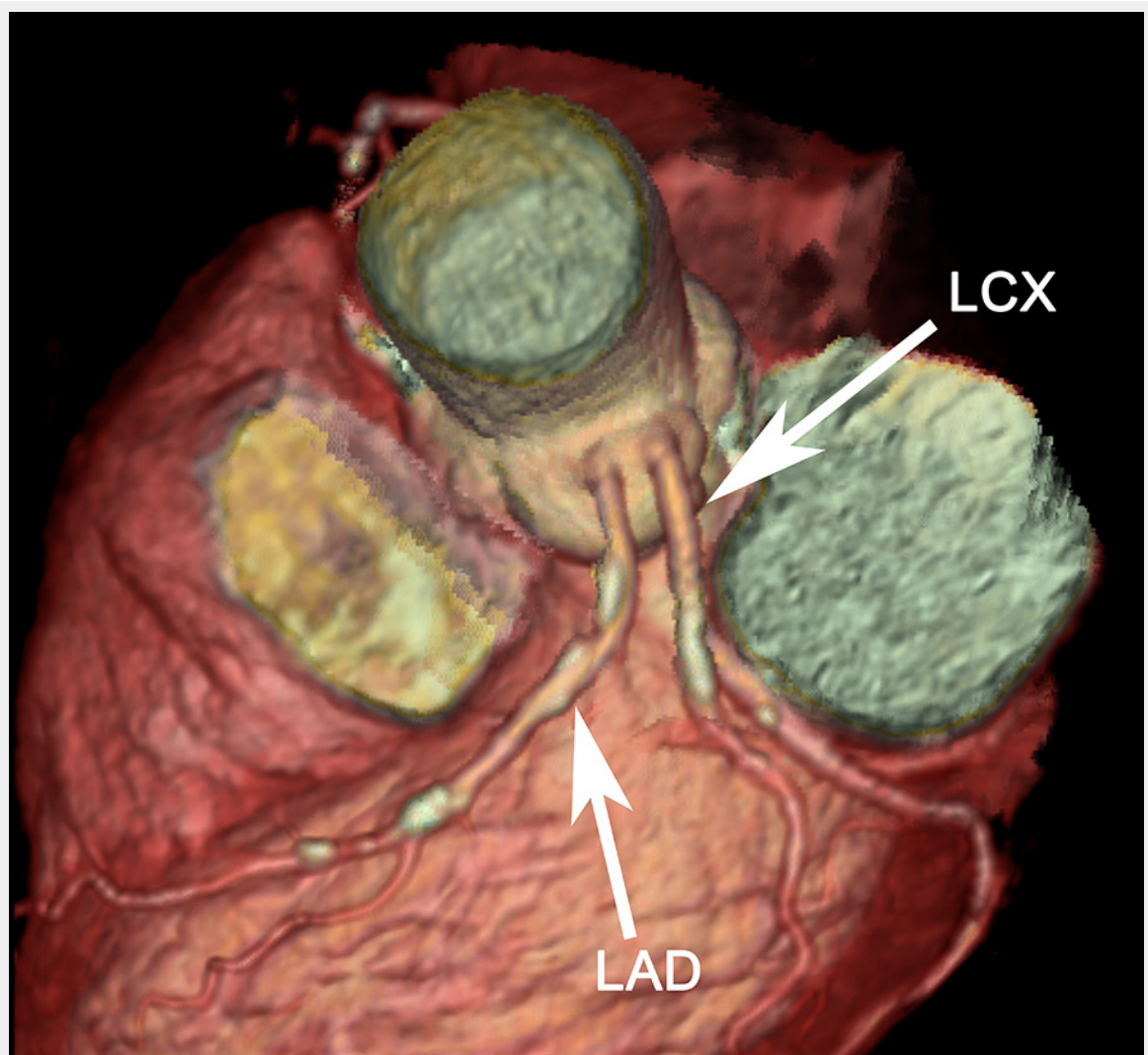


Figure 5

CCTA of a 63-year-old male shows obstructive CAD and absent left main stem with separate ostium for LAD and LCX. Absent left main stem is considered a benign variant of CAA, but the finding may be of clinical importance for eventual revascularisation procedures.

CAA = coronary artery anomaly; CAD = coronary artery disease; CCTA = coronary computed tomography angiography; LAD = left anterior descending artery; LCX = left circumflex coronary artery